UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/311,428	05/13/99	O CONNOR J	54205-B/JPW/

HM12/0117

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EXAMINER	
COOK, L	
ART UNIT	**PAPER NUMBER**
1641	11

DATE MAILED: 01/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/311,428	O CONNOR ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-80* is/are rejected.

7)☒ Claim(s) *69* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicants' Amendment in response to the Restriction Requirement mailed 15 June 2000O in Paper #7 is acknowledged. Applicants have canceled claims 1-5 and 58-66 without prejudice or disclaimer. New claims 67-80 were added by Amendment-B, filed 11/20/00. According, the subject matter of claims 67-80, which recite a "method for detecting gestational trophoblast malignancy" is elected with traverse by the Applicant.

2. Currently, claims 67-80 are pending and under consideration.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does contain the required first sentence of the specification referencing the priority claim. However, it is noted that the reference does not clarify the filing date of PCT/US99/02289 as 3 February 1999. It is suggested that the specification be updated to include the cited date (i.e. page 1, line 7 – International Application No. PCT/US99/02289, filed February 3, 1998, which is a continuation-in-part of U.S. Serial No. 09/017,976, filed February 3, 1998".

Drawings

4. The drawings in this application have been objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449, cited the references they have not been considered. (For example see pages 87 –100).

Oath/Declaration

6. A new oath or declaration is required. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

The oath filed 12/01/99 and 2/28/00, list priority document No. 09/017,976 and PCT/US99/02289 with corresponding filing date as 3 February 1999. The correct filling date for Application No. 09/017,976 should be 3 February 1998. Appropriate correction is required.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. The abstract of the disclosure is objected to because of the following informalities:

A. The first page of the specification should be numbered.

B. Supply a detailed description for Figure 7 which specifically identifies 7A and 7B.

Correction is required. See MPEP § 608.01(b).

9. The use of trademarks has been noted in this application (For example see "Superose" on page 12, line 18). They should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

10. Claim 69 step 2 (vi) is mis-numbered and should be step (v). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 67-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 67, 68, 69, and 70 are vague and indefinite in utilizing the term "suitable" in suitable sample. It is not clear as to what limitation is being placed on the sample type. As recited the metes and bounds of the claim can not be determined. It is suggested that definite language replace "suitable" wherein Applicants intended meaning can be clearly understood.

B. Claims 67(ii), 68(ii), 69(ii), and 70(ii) recites the limitation "first portion and second portion" in "step 1". However, step 1 is directed to a suitable sample and does not distinctly refer to sample portions. There is insufficient antecedent basis for this limitation in the claim.

C. Claims 67, 68, 69, and 70 have improper antecedent support in reciting "immobilizing capturing antibody". Insert ---a---before "capturing" for proper antecedent basis.

D. Claims 67, 68, 69, and 70 are indefinite in reciting "any" in step (ii) because it is unclear what is encompassed by the term "any". Deleting "any" and inserting ---the--- is suggested but not required so as to obviate indefiniteness and provide proper antecedent basis in the claims.

E. The phrase "continued high ratio" in claims 67(4), 68(4), 69(4), and 70(4) employs the relative terms "continued" and "high" which are not defined by the claims. The specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

F. In claims 71, 72, 73, and 74 the parenthetical symbols render the claims indefinite because it is unclear whether the limitation inside the parenthesis is part of the claimed invention.

G. Claims 72 and 74 are vague and indefinite in reciting step (C) because no such step was previously claimed.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 71-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of hybridoma cell lines and monoclonal antibodies B108, B109, B152, and B207 in accordance with 37 CFR 1.801-1.809. While the specification provides enough information for one ordinary skill in the art to produce hybridoma cell lines and monoclonal antibodies with the same or similar properties of and monoclonal antibodies produced by the same (B108, B109, B152, and B207), reproduction of identical cell lines and antibodies is an extremely unpredictable event. Because it does not appear that the monoclonal antibodies and their corresponding hybridoma cell lines, are known and publicly available or can be reproducibly isolated from nature without undue experimentation, a suitable deposit of the hybridoma cell lines and monoclonal antibodies for patent purposes is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §§ 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants, assignees or a statement by an attorney

of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

Amendment of the specification to recite the current practice requiring that a statement concerning all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this Application and that the deposit will be replaced if viable samples cannot be dispensed by the depository made in the instant Application. Without such a statement, it would be impossible for the skilled artisan to practice the invention of claims 71-74 because the specific deposits cannot be placed into the hands of the artisan because other clones made from the source material have no predictable reasonable expectation of success of being identical to the single clone deposited.

Furthermore, unless the deposit was made at or before the time of filing, a declaration filed under 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know should identify the deposited hybridomas and monoclonal antibodies by its depository accession number, establishes that the deposited hybridomas and monoclonal antibodies are the same as that described in the specification, and establish that the deposited hybridomas and monoclonal antibodies were in applicants' possession at the time of filing.

Applicant's attention is directed to In re Lundak, 773 F.2d.1216, 27 USPQ 90 (CAFC 1985) and 37 CRF §§ 1.801-1.809 for further information concerning deposit practice.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claim 67-80 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53-81 of copending Application No. 09/017,976. Although the conflicting claims are not identical, they are not patentably distinct from each other because The instant claims are not patentably distinct from the claims found in co-pending Application No. 09/017,976 because the claims employ the same method steps that encompass obvious modifications in assay design while utilizing the exact same reagents (i.e. molecular isoforms of hCG, non-nicked hCG, B152, B109, and B108). Although one preamble recites "A method of predicting pregnancy outcome – 09/017,976" and the other preamble recites "A method of detecting gestational trophoblast malignancy – 09/311,428", the preambles are encompass the same subject matter and are not given patenatable weight. See MPEP 2111.02 Weight of Preamble

PREAMBLE IS NONLIMITING UNLESS IT BREATHES LIFE AND MEANING INTO THE CLAIM
The preamble is not given the effect of a limitation unless it breathes life and meaning into the claim. In order to limit the claim, the preamble must be "essential to point out the invention defined by the claim." Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951) (discussed below). In claims directed to articles and apparatus, any phraseology in the preamble that limits the structure of that article or apparatus must be given weight. In re Stencel, 828 F.2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987) (discussed below). On the other hand, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) (process claims, discussed below); Kropa v. Robie, 187 F.2d at 152, 88 USPQ at 481 (claims directed to apparatus, products, chemical structure, etc., as discussed below).
In In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976), the claim preamble set forth "A process for preparing foods and drinks sweetened mildly, and protected against discoloration, Streckler's reaction, and moisture absorption." The body of the claim recited two steps directed to the formation of high purity maltose and a third step of adding the maltose to foods and drinks as a sweetener. The court held that the preamble was only directed to the purpose of the process, the steps could stand alone and did not depend on the preamble for completeness.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 67-80 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 09/017,976 which has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this

rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Please Note: In the following rejections, the detection of gestational trophoblast malignancy is seen as intended use for methods detecting and evaluating non-nicked hCG and molecular isoforms of hCG in pregnancy/gestational diagnosis.

I. Claims 67-70, 73, 74, and 75-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellish et al. (Human Reproduction, 1996).

Ellish et al. teach an immunoradiometric assay which has two solid-phase immobilized capture antibodies and one detection antibody to study early pregnancy loss. Ellish et al. employ B109 to capture the non-nicked hCG molecule and B207 to capture free β subunit and hCG free β core fragment. Ellish et al. utilized B108 as the radioactive labeled detection antibody. (page 4074, column 2) .

Although this reference does not specifically state that the assay will be repeated in order to determine continued high ratios as required in the repeating step (4) it is well known to those with ordinary skill in the art that sampling at various points with multiple parameters is commonly used for in assay systems. Methods for determining this data can be achieved by procedures known to those of ordinary skill in the art..

It would have been prima facie obvious to one of ordinary skill in the art to repeat the sample analyses on samples sets and compare them to each other to evaluate the end result s in the method demonstrated by Ellish et al. with a reasonable expectation of success and little additional labor because this information can be easily determined utilizing protocols/data points/etc. that are already being used in their methods, such as range sampling on various days of gestation (i.e. HCG concentrations on day 3, day 2 – see Abstract). The repetition of samples in the method of Ellish et al. would have been an obvious modification to the existing method. One of ordinary skill in the art would utilize various comparative calculations for the resulting

data sets to evaluated the particular diagnosis. These calculations are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to repeat sample analysis on a given sample in the given method to determine the unknown diagnosis as a means of optimizing the assays provided by the art.

II. Claims 67-70, 72, 74, and 75-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birken et al. (Endocrinology 1993).

Birken et al. disclose a two-site immunoradiometric assay to evaluate immunoptency of nicked hCG. Birken et al. further teach a capture antibody that specifically binds non-nicked hCG (intact hCG heterodimer) along with a detecting (tracer) antibody. The capture antibody is B109 and the I125 radiolabeling antibody is B108. (See page 1391, column 1).

Although this reference does not specifically state that the assay will be repeated in order to determine continued high ratios as required in the repeating step (4) it is well known to those with ordinary skill in the art that sampling at various points with multiple parameters is commonly used for in assay systems. Methods for determining this data can be achieved by procedures known to those of ordinary skill in the art..

It would have been prima facie obvious to one of ordinary skill in the art to repeat the sample analyses on samples sets and compare them to each other to evaluate the end result s in the method demonstrated by Birken et al. with a reasonable expectation of success and little additional labor because this information can be easily determined utilizing protocols/data

points/etc. that are already being used in the cited method. The repetition of samples in the method of Birken et al. would have been an obvious modification to the existing method. One of ordinary skill in the art would utilize various comparative calculations for the resulting data sets to evaluated the particular diagnosis. These calculations are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to repeat sample analysis on a given sample in the given method to determine the unknown diagnosis as a means of optimizing the assays provided by the art.

III. Claims 67-70, 72, 74, and 75-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over by O.Connor et al. (Cancer Research, 1988).

O'Connor et al. disclosed assays to evaluate hCG function. O'Connor et al. specifically teach immobilized capture antibodies via B108 or B109 coated solid phase materials which specifically bind non-nicked hCG. (See page 1362, column 1).

Although this reference does not specifically state that the assay will be repeated in order to determine continued high ratios as required in the repeating step (4) it is well known to those with ordinary skill in the art that sampling at various points with multiple parameters is commonly used for in assay systems. Methods for determining this data can be achieved by procedures known to those of ordinary skill in the art..

It would have been prima facie obvious to one of ordinary skill in the art to repeat the sample analyses on samples sets and compare them to each other to evaluate the end results in

the method demonstrated by O.Connor et al. with a reasonable expectation of success and little additional labor because this information can be easily determined utilizing protocols/data points/etc. that are already being used in their methods, such as range sampling to determine Inter- and Intra-assay variation (1362 – Quality Control Evaluation of Immunoassay). The repetition of samples in the method of O.Connor et al. would have been an obvious modification to the existing method. One of ordinary skill in the art would utilize various comparative calculations for the resulting data sets to evaluated the particular diagnosis. These calculations are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to repeat sample analysis on a given sample in the given method to determine the unknown diagnosis as a means of optimizing the assays provided by the art.

Allowable Subject Matter

17. Currently claim 71 is free of the prior art of record which neither teach or suggest the instant molecular isoform of hCG or a characteristic epitope thereof defined by the specific binding of monoclonal antibody B152. Claim 71 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

18. For reasons aforementioned, no claims are allowed.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7D16
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